Original Article

Effect of Ranibizumab in Patients with Treatment-Naïve Retinopathy of Prematurity

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Abstract

Objectives: To determine the effect of intravitreal ranibizumab (IVR) in patients with treatment-naïve retinopathy of prematurity (ROP) in terms of disease regression and need for rescue therapy.

Materials and Methods: This study evaluated disease regression and rescue therapy requirement in treatment-naïve ROP cases treated with IVR. Among 188 screened patients, 80 had ROP. Thirty-eight patients (76 eyes) with type 1 ROP and aggressive ROP (AROP) were included. Treatment involved a single dose of 0.2 mg ranibizumab injected under aseptic conditions. Patients were monitored post-treatment for up to 6 months. Recurrence of disease was managed with argon laser photocoagulation targeting the peripheral avascular retina. Data analysis utilized t-tests for continuous variables and χ^2 tests for categorical data, with a significance threshold of $p<0.05$.

Results: The study included 19 males and 19 females, with 56 eyes having AROP and 20 eyes with type 1 ROP. All AROP cases required rescue therapy, with a mean interval of 3.43±0.84 weeks between treatments. Sixty percent of type 1 ROP eyes also needed laser therapy. While type 1 ROP cases had slightly higher gestational age and lower birth weight compared to AROP, these differences were not statistically significant ($p=0.081$ and $p=0.27$, respectively). However, the interval between treatments was significantly longer in type 1 ROP than in AROP ($p=0.0016$).

Conclusion: Ranibizumab demonstrated effectiveness in initial disease regression but was linked to reactivation in all AROP and 60% of type 1 ROP cases, highlighting the importance of more frequent follow-ups after ranibizumab injection, particularly for AROP patients.

Keywords: Ranibizumab, retinopathy of prematurity, bevacizumab, anti-vascular endothelial growth factor

Introduction

The foundation for using intravitreal bevacizumab in the treatment of retinopathy of prematurity (ROP) was established by the "Bevacizumab Eliminates the Angiogenic Threat for Retinopathy of Prematurity" (BEAT-ROP) trial.[1] More recent evidence on the use of intravitreal ranibizumab (IVR) comes from the "Ranibizumab Compared with Laser Therapy for the Treatment of Infants Born Prematurely With Retinopathy of Prematurity" trial.[2] In 2019, ranibizumab was approved by the European Medicines Agency at a dose of 0.20 mg for the treatment of ROP. Since then, the treatment approach has continued to evolve due to the varying disease patterns observed across different regions worldwide. Literature indicates that anti-vascular endothelial growth factor (anti-VEGF) treatment tends to result in recurrence.[3] Additionally, in developing countries, ROP has been reported in infants with higher birth weights and gestational ages (GA), highlighting disease patterns that differ from those in the developed world.[4] This underscores the need for data from these regions to better understand how the disease responds to treatment in these areas. This study aimed to evaluate the efficacy of IVR in treatment-naïve ROP patients from a tertiary care center in a developing Southeast Asian country.

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Materials and Methods

This quasi-experimental study was conducted in the ophthalmology department of Lahore General Hospital from July to December 2024. Ethical approval was obtained from the Lahore General Hospital Review Board (IRB number: LGH/297/24, dated: 09.07.2024). The study strictly followed the Declaration of Helsinki, and verbal informed consent was obtained from the parents of all patients before examination and at the start of examination and treatment. Of 188 preterm infants screened during the study period, 80 infants had ROP. For preterm infants born at or before 32 weeks of gestation, oxygen concentration was kept between 91% and 95%.

Based on an ROP prevalence of 27% among preterm infants in a local study,[5] an 80% confidence interval, and 5% margin of error, the required sample size was determined using the formula $n=Z^2\ p\cdot(1-p)/d^2$, where Z = Z-score corresponding to the desired confidence level (for 80% confidence, Z=1.28), p = Estimated prevalence (27% or 0.27), and d = Margin of error (5% or 0.05). According to the result of this calculation, the minimum number of infants to screen was 129.

We screened 188 infants to address dropouts. Out of these, 80 infants were diagnosed with ROP. Screening was conducted following the Pakistan Retinopathy of Prematurity Education and Research Alliance protocols, which include all premature infants born at ≤35 weeks of GA or weight ≤2000 grams. Disease staging was performed using an indirect ophthalmoscope with a 20 D lens and RetCam. Dilating drops were prepared by mixing 0.5 cc of 10% phenylephrine (Mediphrine, Medipak, Pakistan), 1 cc of 1% cyclopentolate (Cyclopen, Ethical, Pakistan), and 3.5 cc of artificial tears (Tears Plus, Allergan, Pakistan). Type 1 ROP was defined as:

- Zone I: any stage ROP with plus disease
- Zone I: stage 3 ROP without plus disease
- Zone II: stage 2 or 3 ROP with plus disease

Treatment-naïve preterm infants with type 1 ROP or aggressive posterior ROP (AROP) defined were included. AROP was defined according to the International Classification of ROP 3rd edition (ICROP3).[6]

Patients with systemic disease, sepsis, and unstable respiratory status were excluded. All patients with type 1 ROP or AROP received IVR within 72 hours of the diagnosis. Strict aseptic protocols were followed in a standard ophthalmic operating room. A drop of 5% of povidone-iodine (Pyodine, Brookes Pharmaceutical Labs [Pvt] Ltd, Pakistan) was instilled in the conjunctival sac. The eye was stabilized using toothed forceps, and the injection was administered 1.5 mm posterior to the limbus, while carefully avoiding injury to the lens. A dose of 0.2 mg/0.02 mL ranibizumab (Patizra, Novartis Pharmaceuticals) was injected. After the injection, a moxifloxacin antibiotic eye drop (Vigamox, Alcon, Pakistan) was instilled and the speculum was removed. Moxifloxacin eye drops (Vigamox) were prescribed four times a day for 5 days. Indirect ophthalmoscopy was performed to assess the perfusion of the central retinal artery and to check for iatrogenic retinal tears or vitreous hemorrhage. Patients were followed up on day 1 post-treatment and subsequently at weekly intervals, depending on their response, for up to 6 months.

The primary outcome measures included disease regression with resolution of neo-vessels and disappearance of the ridge; recurrence of ROP; and any associated complications. Regression and reactivation were defined as per ICROP3.[6] Regression was considered when the disease showed signs of involution and resolution, whereas reactivation was defined as recurrence of the features of acute phase.

The criteria for rescue therapy were:

- New vessels at the junction of vascularized and avascular retina, or in the vitreous.
- Vascular dilation and tortuosity of the posterior pole vessels.
- Fibrous tissue growth, often at the border of vascular and avascular retina.
- Localized traction due to new fibrovascular proliferation.
- A large area of the peripheral retina remains avascular and ischemic.

In cases of disease reactivation, argon laser photocoagulation to the peripheral avascular retina was performed as secondary treatment.

Statistical Analysis

Data collection was conducted using RetCam software, an Excel spreadsheet, and a form designed specifically for this study. Variables with a normal distribution were analyzed using t-tests, while categorical variables were assessed using chi-square tests. Quantitative data was evaluated in terms of percentages and frequencies, with a p value of <0.05 considered statistically significant.

Results

During the study period, 188 patients were screened and 80 infants had ROP. Among these, 28 infants (56 eyes) had AROP and 10 (20 eyes) had type 1 ROP (total 76 eyes). There were 19 males and 19 females. The mean GA was 31.56±2.64 weeks (range, 20-37). Mean birth weight was 1487.85±394.75 g (range, 700-2500) and the first injection was given at a mean GA of 36.86+2.5 weeks (range, 29-41). Rescue therapy was given at 41.41±2.79 weeks (range, 32-46).

Laser treatment was performed as rescue therapy in eyes with incomplete regression after IVR. All patients with AROP needed rescue therapy, with a mean interval between the two therapies of 3.43±0.84 weeks (range, 2-6). Sixty percent of eyes with type 1 ROP also required rescue therapy. Figure 1 shows regression of AROP 4 weeks after IVR. Figures 2 and 3 show premature infants with type 1 ROP. Clinical and treatment details are given in Table 1.

A comparison between the eyes with AROP and type 1 ROP revealed a slightly higher average GA in the type 1 ROP group, but the difference was not statistically significant (p=0.081). Similarly, the average birth weight was slightly lower in the type 1 ROP group, but not significantly (p=0.27). Notably, the interval between the two therapies was significantly longer in the type 1 ROP cases compared to the AROP group (p=0.0016).

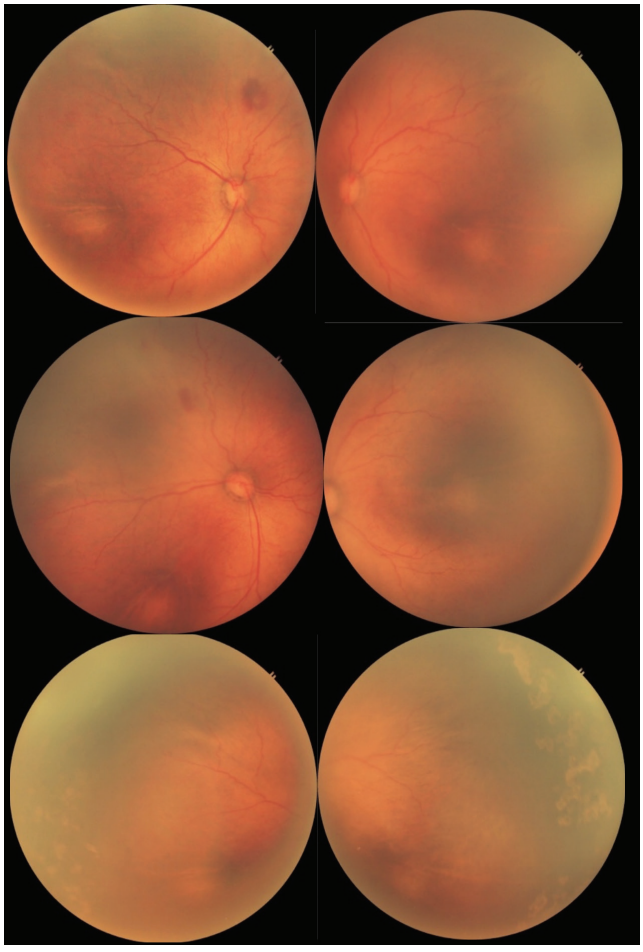

Figure 1. Top, first visit of an infant born at 32 weeks of gestation and 1200 grams, showing aggressive retinopathy of prematurity. Middle, image enhancement. Bottom, regression 4 weeks after intravitreal ranibizumab in both eyes

Discussion

Our results demonstrated that patients receiving IVR for ROP required rescue therapy in 100% of AROP cases and 60% of type 1 ROP cases. These findings are consistent with the previous literature, which highlights disease reactivation as a common occurrence. For instance, Stahl et al.[3] reported late reactivation in 14% of infants treated with two initial injections.

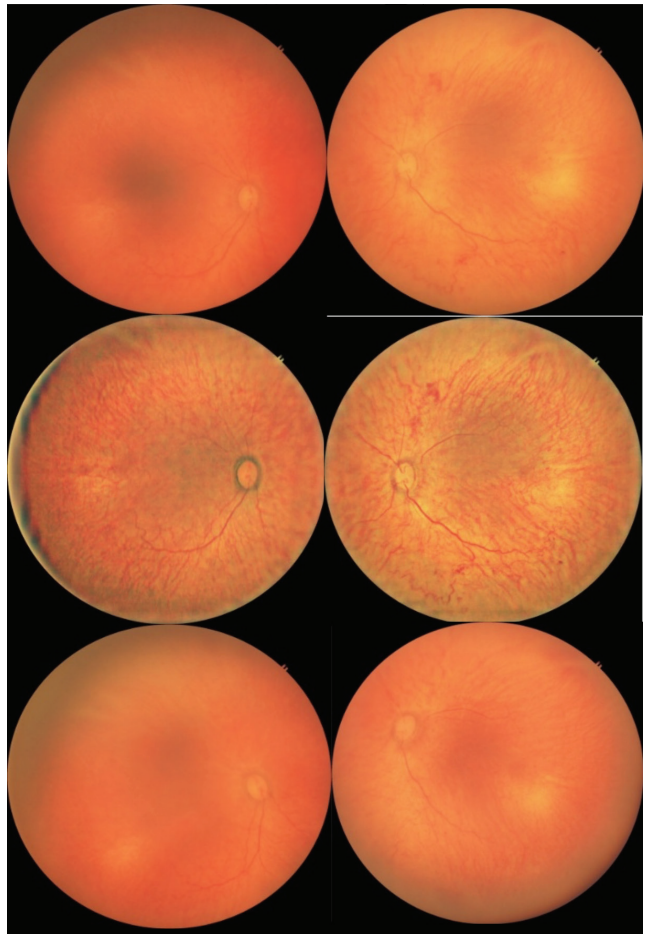

Figure 2. Top, first visit of a premature infant born at 1100 grams and 27 weeks of gestation, exhibiting zone 2, stage 3 with plus disease. Middle, incomplete regression after intravitreal ranibizumab. Bottom, appearance after laser treatment for reactivation

Table 1. Comparison of clinical and treatment characteristics between patients with AROP and type 1 ROP

Parameter	AROP (n=56) (range)	Type 1 ROP (n=20) (range)	p value
Mean gestational age (GA) at birth, weeks	30.71±3.57 (20-34)	32.4±1.71 (30-37)	0.081
Mean birth weight, grams	1535.7±433 (700-2500)	1440±356.5 (1000-2000)	0.27
Mean GA at first injection, weeks	35.71±2.84 (29-39)	38±2.2 (36-41)	0.014*
Mean GA at rescue therapy, weeks	39.14±2.69 (32-41)	43.67±2.88 (40-46)	0.0004*
Mean interval between initial and rescue therapy, weeks	3.43±0.84 (2-4)	4.67±1.03 (4-6)	0.0016*
Percentage of eyes requiring laser	100%	60%	0.0033*

*p<0.05, ROP: Retinopathy of prematurity, AROP: Aggressive retinopathy of prematurity

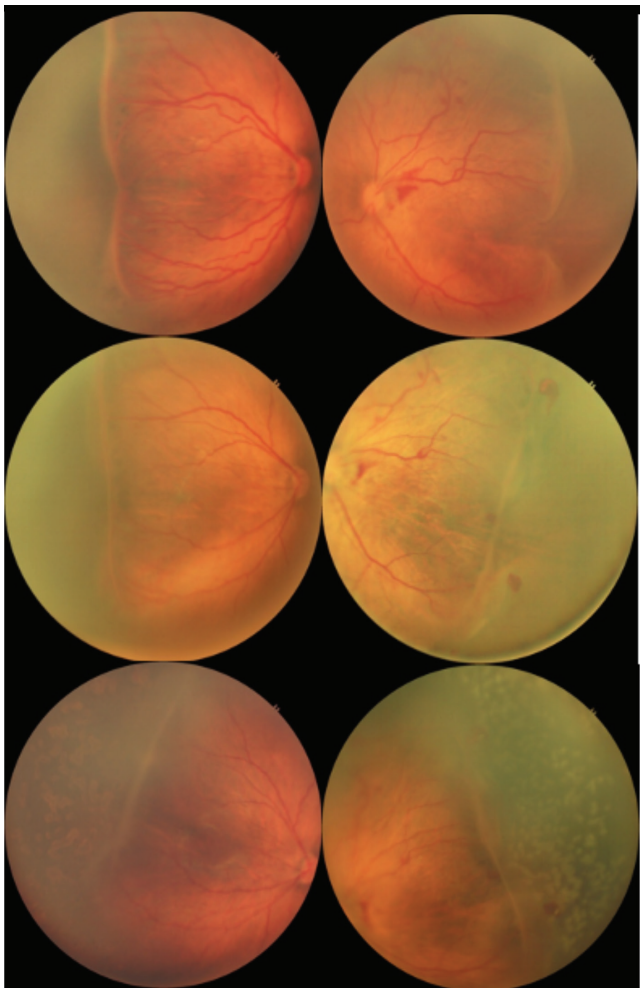

Figure 3. Infant with birth weight of 1800 grams and gestational age of 29 weeks, exhibiting zone 2 posterior, stage 3 disease. Top, before intravitreal ranibizumab injection. Middle, post-injection. Bottom, appearance after laser treatment to the avascular retina due to incomplete regression

Disease regression was observed by week 5 post-injection, but reactivation occurred at week 6, necessitating re-treatment. After subsequent treatments, the disease remained inactive for 8 weeks but reactivated again at week 10. A third injection administered 17 weeks after the initial injection showed slower regression, although the treated eyes displayed no signs of ROP. In contrast, our patients showed initial regression for 3.43±0.84 weeks in AROP and 4.67±1.03 weeks in type 1 ROP. After that we had to opt for rescue therapy in the form of laser photocoagulation. As the disease reactivated within a few weeks, we avoided a second injection owing to the systemic absorption of ranibizumab, which could result in cumulative systemic effects.

The management of ROP has evolved significantly with the advent of anti-VEGF therapies, which offer targeted regression of abnormal vascular proliferation. In this case, IVR has demonstrated substantial efficacy in inducing initial regression of ROP, with studies reporting regression rates exceeding 75% in treated eyes. In our study the initial regression was seen in all patients, but the effect was not long lasting. Thus, we find that recurrence remains a notable concern. While some studies observed recurrence rates as high as 41.5%, others, like Bassiouny et al.[7], reported a significantly lower recurrence rate of 2.3%. The variability in recurrence rates can be attributed to differences in inclusion criteria, dosage, and follow-up protocols. For example, Wong et al.[8] found that recurrence with IVR typically occurred between 41 and 42 weeks of postmenstrual age (PMA), emphasizing the need for vigilant follow-up during this critical period.

A retrospective review by Sahinoglu-Keskek et al.[9] analyzed 15 eyes of 8 premature infants with AROP treated initially with IVR. Reactivation occurred at a median of 5 weeks post-injection, and only two eyes required a second IVR injection. These findings align with our study, which highlighted shorter reactivation intervals in AROP. However, laser photocoagulation for recurrence provided favorable outcomes in our cases.

Extended follow-up is needed after IVR as late recurrence is shown up to 35 weeks after anti-VEGF injection or 69 weeks PMA.[10,11] Longer follow-up is particularly crucial in high-risk cases, such as those with zone I ROP, low Apgar scores, and multiple births.

Our cases of AROP had 100% recurrence. However, Ling et al.[12] reported a recurrence rate of 20.8% in the IVR group and an 8.3±1.6-week mean interval to recurrence.

With the advent of new anti-VEGF drugs, comparative studies of different anti-VEGF indicate that conbercept and ranibizumab are both effective for treating ROP, but conbercept is associated with less recurrence and longer intervals between treatments.[13] On the other hand, in a multicenter prospective trial, recurrence rates were similar between conbercept (16.67%) and ranibizumab (23.34%).[14] However, the interval to reactivation was longer than in our cohort.

Initial regression was seen in all patients in our study. However, Xu et al.[15] reported a failure rate of 11%, with management involving repeat injections, laser therapy, vitrectomy, or combinations thereof. The most common manifestations of treatment failure included recurrent plus disease and stage 3 ROP. Aflibercept has demonstrated longer efficacy with lower recurrence rates than ranibizumab, as observed in studies by Süren et al.[16] and Lee et al.[17] Bevacizumab, with its longer half-life, also showed a lower recurrence rate but raised concerns about systemic side effects.

Recent studies emphasize the need for individualized treatment strategies based on the initial therapy used.[18,19] While IVR is favored for its refractive benefits and anatomical outcomes, repeated use for recurrence should be carefully weighed against the risks of systemic VEGF suppression.

With so many options currently available, the choice of agent often depends on disease severity, the retinal zone involved, and individual patient risk factors. Some studies have compared different doses of IVR in terms of need of re-treatment. Ahmed et al.[20] used low-dose IVR and showed promising results, with complete retinal vascularization and no need for retreatment, though further large-scale studies are required to validate its efficacy and safety.

Although complication rates are higher in laser therapy due to peripheral retinal ablation, the interval between treatment and retreatment is significantly longer than with anti-VEGF agents.[21] On the other hand, the faster action of anti-VEGF agents compared to laser therapy makes them preferable for aggressive cases, especially before 36 weeks of PMA, when laser therapy is associated with higher short-term retinal detachment rates.[22] Higher reactivation risks have been associated with early PMA at treatment and with AROP.[8,23] This holds true to some extent in our study, as patients with AROP had lower GA compared to those with type 1 ROP. Similarly, multivariate analyses identified PMA ≤35 weeks at anti-VEGF therapy and AROP as significant predictors of reactivation.[24]

Optimal timing for adding laser therapy in conjunction with anti-VEGF treatment remains a topic of debate. Kim et al.[25] reported using an 810-nm diode laser within 0 to 8 days post-injection (median 3 days) and observed good outcomes. Others opting for laser intervention in cases of recurrence performed the procedure between 4 and 14 weeks post-injection.[26]

Determining the ideal interval between injection and laser is complex, influenced by factors such as the disease's response to the drug, recurrence patterns, vascular growth into the retina beyond zone 1, infant weight, PMA, systemic conditions, and follow-up compliance. This challenge is particularly pronounced in rural settings, where follow-up compliance can be limited.

Although laser therapy or repeat anti-VEGF injections are valid options, the rationale for delaying laser ablation after anti-VEGF treatment is to allow vascularization to extend beyond the critical zone 1 region. In some cases, vascular growth progresses into more peripheral zones before halting, recurring, or worsening. In our study, we applied laser to the peripheral retina after 4 weeks and spread the laser sessions over multiple visits to allow normal vessels to grow as far as possible.

In a study by Parchand et al.[27], infants with posterior zone I ROP were treated with immediate IVR and zone I-sparing laser ablation at 4 weeks. Combined IVR and zone I-sparing laser ablation were effective in these cases.

Gangwe et al.[28] compared early versus deferred laser therapy in infants with AROP initially treated with IVR. Early laser was performed at 1 week (Group 1), while deferred laser was applied at 6 weeks or earlier if recurrence occurred (Group 2). Structural outcomes were comparable between groups, but deferred laser required fewer spots. In severe cases like AROP, combining IVR with laser therapy has shown promising outcomes. Studies by Kim et al.[25] and Dudani et al.[29] reported successful regression of fibrovascular proliferation and reduced recurrence with this combined approach. However, the timing of laser therapy post-IVR remains critical, as delayed intervention may result in unfavorable outcomes.

One of the benefits of repeated injections is complete vascularization of the retina, which cannot be achieved with laser therapy as described by Xia et al.[30] They found that 54.3% of patients achieved complete vascularization after repeated injections, with GA over 29 weeks being a significant predictor of complete vascularization.

The shorter systemic half-life of ranibizumab compared to other anti-VEGF agents, such as bevacizumab, contributes to its higher recurrence rate. Despite this, IVR's effectiveness in achieving complete retinal vascularization after subsequent injections underscores its utility as a primary and secondary treatment modality.

A significant challenge in ROP management is addressing persistent avascular retina (PAR), a condition observed in 22-38% of eyes treated with anti-VEGF therapy. PAR poses long-term risks, including retinal detachment and vascular abnormalities. Thus, long-term follow-up is imperative for infants treated with IVR to monitor for late recurrences and vascular changes.

Study Limitations

This study highlights the clinical outcomes, challenges, and therapeutic strategies associated with IVR in ROP treatment, supported by evidence from various other studies. The limitations include a short follow-up, which does not address long-term outcomes and the possibility of delayed reactivation of the disease beyond six months. Considering the systemic absorption of the drug, only a single injection was given in this study, and rescue therapy consisted of laser therapy instead of repeat IVR. Lack of a control group and patients from a single center limits the study's generalizability to different populations or healthcare settings. These limitations suggest that while ranibizumab may show promise for initial disease regression in ROP, further research with larger, more diverse populations and longer follow-up periods would be required to establish its long-term effectiveness and safety in treating ROP.

Conclusion

IVR offers a powerful option for managing ROP, particularly in zone I disease and AROP. Despite challenges like recurrence and PAR, its benefits in terms of anatomical outcomes make it a cornerstone in ROP treatment. Continued advancements in anti-VEGF therapies and combination strategies hold promise for improving outcomes in this vulnerable population.

Ethics

Ethics Committee Approval: Ethical approval was obtained from the Lahore General Hospital Review Board (IRB number: LGH/297/24, dated: 09.07.2024).

Informed Consent: Informed consent was obtained from the parents of all patients before examination and at the start of examination and treatment.

Declarations

Authorship Contributions

Surgical and Medical Practices: H.K., T.G.M., A.A., I.K., S.M., Concept: H.K., T.G.M., A.A., I.K., S.M., Design: H.K., T.G.M., Data Collection or Processing: H.K., T.G.M., A.A., I.K., S.M., Analysis or Interpretation: H.K., T.G.M., Literature Search: H.K., T.G.M., Writing: T.G.M.

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References

1. Mintz-Hittner HA, Kennedy KA, Chuang AZ; BEAT-ROP Cooperative Group. Efficacy of intravitreal bevacizumab for stage 3+ retinopathy of prematurity. N Engl J Med. 2011;364:603-615.
2. Stahl A, Lepore D, Fielder A, Fleck B, Reynolds JD, Chiang MF, Li J, Liew M, Maier R, Zhu Q, Marlow N. Ranibizumab versus laser therapy for the treatment of very low birthweight infants with retinopathy of prematurity (RAINBOW): an open-label randomised controlled trial. Lancet. 2019;394:1551-1559.
3. Stahl A, Bründer MC, Lagrèze WA, Molnár FE, Barth T, Eter N, Guthoff R, Krohne TU, Pfeil JM; CARE-ROP Study Group. Ranibizumab in retinopathy of prematurity - one-year follow-up of ophthalmic outcomes and two-year follow-up of neurodevelopmental outcomes from the CARE-ROP study. Acta Ophthalmol. 2022;100:e91-e99.
4. Sadiq MA, Karamat I, Khan AA. Retinopathy of prematurity in Pakistan. J AAPOS. 2016;20:541-542.
5. Rauf A, Saigol HK, Chauhan K, Akbar S, Chaudhary NI. Prevalence of retinopathy of prematurity in premature neonates visiting Sir Gangaram Hospital Lahore. 2023. Pak J Med Health Scie. 2023;17:206.
6. Chiang MF, Quinn GE, Fielder AR, Ostmo SR, Paul Chan RV, Berrocal A, Binenbaum G, Blair M, Peter Campbell J, Capone A Jr, Chen Y, Dai S, Ells A, Fleck BW, Good WV, Elizabeth Hartnett M, Holmstrom G, Kusaka S, Kychenthal A, Lepore D, Lorenz B, Martinez-Castellanos MA, Özdek Ş, Ademola-Popoola D, Reynolds JD, Shah PK, Shapiro M, Stahl A, Toth C, Vinekar A, Visser L, Wallace DK, Wu WC, Zhao P, Zin A. International Classification of Retinopathy of Prematurity, Third Edition. Ophthalmology. 2021;128:e51-e68.
7. Bassiouny RM, Gaafar WM, El Nokrashy A, Abdelhameed AG, Attallah EA, Elgharieb AG, Bassiouny MR. Clinical outcome following reinjection of ranibizumab for reactivation of retinopathy of prematurity. Eye (Lond). 2022;36:2137-2143.
8. Wong RK, Hubschman S, Tsui I. Reactivation of retinopathy of prematurity after ranibizumab treatment. Retina. 2015;35:675-680.
9. Sahinoglu-Keskek N, Akkoyun I, Torer B. Favorable outcomes in the treatment of aggressive posterior retinopathy of prematurity. Eur J Ophthalmol. 2021;31:179-183.
10. Hu J, Blair MP, Shapiro MJ, Lichtenstein SJ, Galasso JM, Kapur R. Reactivation of retinopathy of prematurity after bevacizumab injection. Arch Ophthalmol. 2012;130:1000-1006. Erratum in: Arch Ophthalmol. 2013;131:212.
11. Mintz-Hittner HA, Geloneck MM, Chuang AZ. Clinical management of recurrent retinopathy of prematurity after intravitreal bevacizumab monotherapy. Ophthalmology. 2016;123:1845-1855.
12. Ling KP, Liao PJ, Wang NK, Chao AN, Chen KJ, Chen TL, Hwang YS, Lai CC, Wu WC. Rates and risk factors for recurrence of retinopathy of prematurity after laser or intravitreal anti-vascular endothelial growth factor monotherapy. Retina. 2020;40:1793-1803.
13. Cheng Y, Zhu X, Linghu D, Liang J. Comparison of the effectiveness of conbercept and ranibizumab treatment for retinopathy of prematurity. Acta Ophthalmol. 2020;98:e1004-e1008.
14. Wu FY, Yu WT, Zhao DX, Pu W, Zhang X, Gai CL. Recurrence risk factors of intravitreal ranibizumab monotherapy in retinopathy of prematurity: a retrospective study at one center. Int J Ophthalmol. 2023;16:95-101.
15. Xu Y, Deng G, Zhang J, Zhu J, Liu Z, Xu F, Zhou D. Efficacy of four anti-vascular endothelial growth factor agents and laser treatment for retinopathy of prematurity: a network meta-analysis. Biomol Biomed. 2023;24:676-687.
16. Süren E, Özkaya D, Çetinkaya E, Kalaycı M, Yiğit K, Kücük MF, Erol MK. Comparison of bevacizumab, ranibizumab and aflibercept in retinopathy of prematurity treatment. Int Ophthalmol. 2022;42:1905-1913.
17. Lee CC, Chiang MC, Chu SM, Wu WC, Ho MM, Lien R. Clinical risk factors for retinopathy of prematurity reactivation after intravitreal antivascular endothelial growth factor injection. J Pediatr. 2024;273:113913.
18. Patel NA, Acaba-Berrocal LA, Hoyek S, Fan KC, Martinez-Castellanos MA, Baumal CR, Harper CA, Berrocal AM; Retinopathy of Prematurity Injection Consortium (ROPIC). Comparison in retreatments between bevacizumab and ranibizumab intravitreal injections for retinopathy of prematurity: a multicenter study. Ophthalmology. 2023;130:373-378.
19. Kubota H, Fukushima Y, Nandinanti AB, Endo T, Nishida K. Retinal blood vessel formation in the macula following intravitreal ranibizumab injection for aggressive retinopathy of prematurity. Cureus. 2024;16:e60005.
20. Ahmed IS, Hadi AM, Hassan HH. Efficacy of ultra-low-dose (0.1 mg) ranibizumab intravitreal injection for treatment of prethreshold type 1 retinopathy of prematurity: a case series. Eur J Ophthalmol. 2020;30:40-47.
21. Wang Z, Zhang Z, Wang Y, Di Y. Effect of ranibizumab on retinopathy of prematurity: a meta-analysis. Front Pharmacol. 2022;13:897869.
22. Barry GP, Yu Y, Ying GS, Tomlinson LA, Lajoie J, Fisher M, Binenbaum G; G-ROP Study Group. Retinal detachment after treatment of retinopathy of prematurity with laser versus intravitreal anti-vascular endothelial growth factor. Ophthalmology. 2021;128:1188-1196.
23. Chan JJT, Lam CPS, Kwok MKM, Wong RLM, Lee GKY, Lau WWY, Yam JCS. Risk of recurrence of retinopathy of prematurity after initial intravitreal ranibizumab therapy. Sci Rep. 2016;6:27082.
24. Iwahashi C, Utamura S, Kuniyoshi K, Sugioka K, Konishi Y, Wada N, Kusaka S. Factors associated with reactivation after intravitreal bevacizumab or ranibizumab therapy in infants with retinopathy of prematurity. Retina. 2021;41:2261-2268.
25. Kim J, Kim SJ, Chang YS, Park WS. Combined intravitreal bevacizumab injection and zone I sparing laser photocoagulation in patients with zone I retinopathy of prematurity. Retina. 2014;34:77-82.
26. Tandon M, Vishal MY, Kohli P, Rajan RP, Ramasamy K. Supplemental laser for eyes treated with bevacizumab monotherapy in severe retinopathy of prematurity. Ophthalmol Retina. 2018;2:623-628.
27. Parchand SM, Agrawal D, Gangwe A, Saraogi T, Agrawal D. Combined intravitreal ranibizumab and zone I sparing laser ablation in infants

with posterior zone I retinopathy of prematurity. Indian J Ophthalmol. 2021;69:2164-2170.

28. Gangwe AB, Agrawal D, Gangrade AK, Parchand SM, Agrawal D, Azad RV. Outcomes of early versus deferred laser after intravitreal ranibizumab in aggressive posterior retinopathy of prematurity. Indian J Ophthalmol. 2021;69:2171-2176.
29. Dudani AI, Dudani AA, Dudani K, Dudani AA. Combination therapy of intravitreal ranibizumab and laser photocoagulation for aggressive posterior retinopathy of prematurity. Indian J Ophthalmol. 2022;70:703-704.
30. Xia F, Lyu J, Peng J, Zhao P. Repeated intravitreal ranibizumab for reactivated retinopathy of prematurity after intravitreal ranibizumab monotherapy: vascular development analysis. Graefes Arch Clin Exp Ophthalmol. 2022;260:2837-2846.